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     (FILE 'HOME' ENTERED AT [redacted])

     FILE 'MEDLINE' ENTERED AT 21:48:31 [redacted]
L1         9601 S SEROS?
L2           93 S L1(5A)(INTACT OR REMAIN? OR KEEP?)
L3            5 S L2 AND GRAFT?

     FILE 'STNGUIDE' ENTERED AT 21:50:57 ON 30 SEP 2004

     FILE 'MEDLINE' ENTERED AT 21:52:03 ON 30 SEP 2004
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L5           78 S L4 AND PY<2001
L6            3 S L5 AND SEED?
L7           75 S L5 NOT L6
L8         1434 S L1(5A)(SIDE OR SURFACE)
L9            2 S L8(10A)GRAFT?
L10          12 S L8 AND GRAFT?
L11          10 S L8 AND SEED?
L12          83 S L8 AND ?CULTUR?
L13           0 S L12 AND SIS
L14          88 S L8 AND SUBMUCOS?
L15          13 S L14 AND (SMOOTH MUSCLE OR BLADDER OR URINARY OR UROTHEL?)
L16           1 S L14 AND TISSUE (5A)ENGIN?
L17         616 S SEROS? AND (SEED? OR ?CULTUR?)
L18          42 (SMOOTH MUSCLE OR BLADDER OR URINARY OR UROTHEL?) AND L17
L19          41 S L18 NOT L15

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L21           2 S L20 AND SEED?
L22           1 S SEROS?(5A)SEED?
L23          20 S SEROS?(5A)?CULTUR?

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L25        3091 S L24(5A)(SIDE OR SURFACE)
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L28          11 S L25 AND SEED?
L29           5 S L25 AND ENGINEER?
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from related

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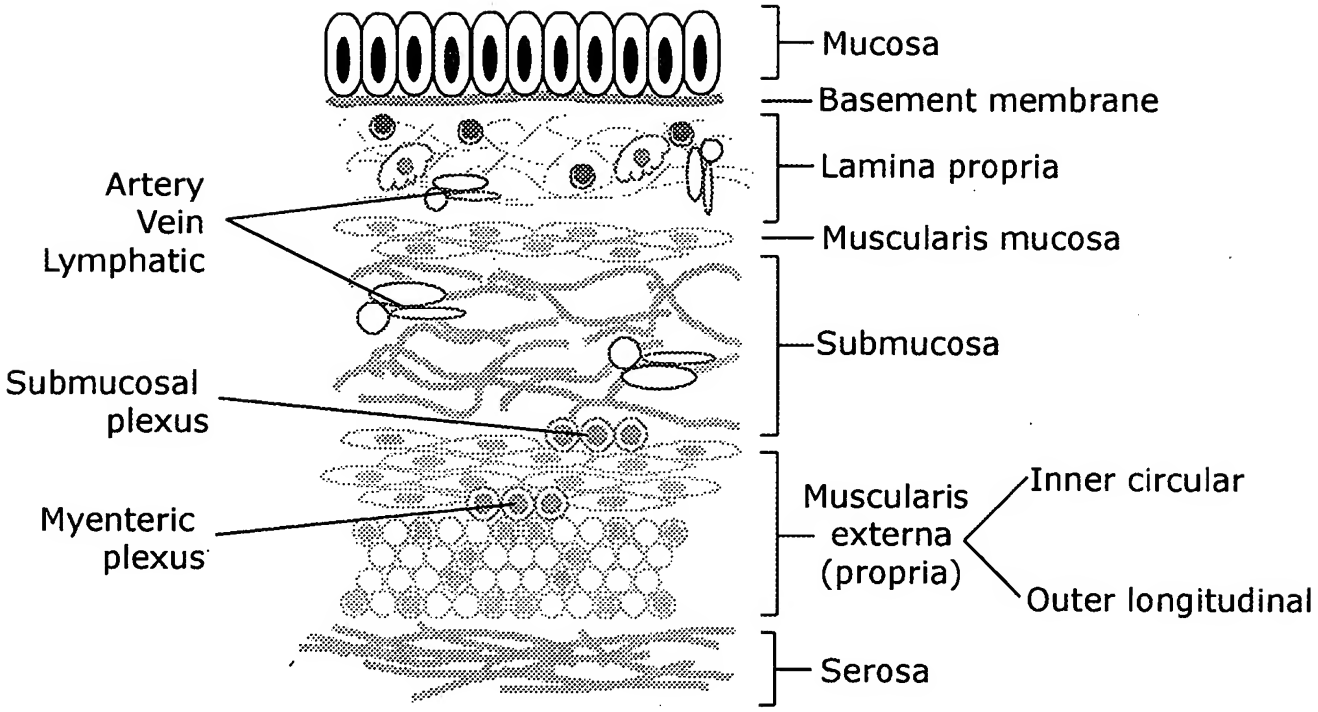
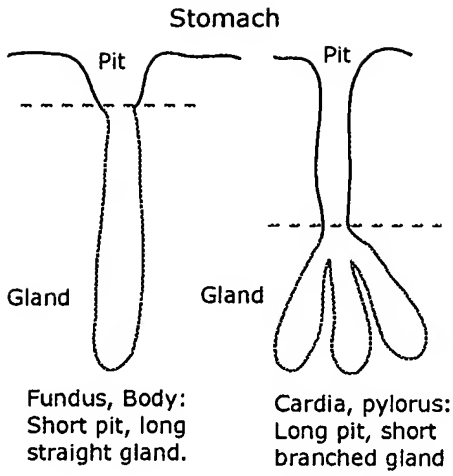
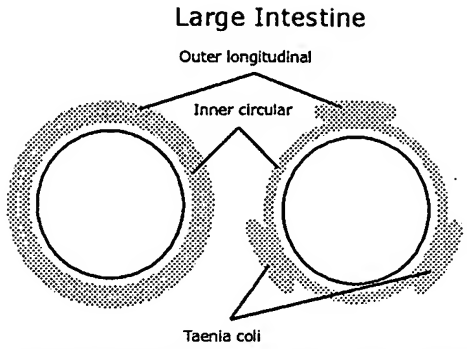


General structure of the gut wall. The mucosa (epithelium) faces the lumen, and is attached to a basement membrane. Beneath is the delicate connective tissue of the lamina propria, within which many immune cells and some connective tissue cells are found. A thin layer of circularly oriented smooth muscle cells, the muscularis mucosa, seperates the lamina propria from the submucosa. The submucosa is made of moderately dense connective tissue, and contains an extensive network of blood vessels and lymphatics. These in turn feed smaller vessels in the lamina propria which in turn supply the extensive capillary beds close to the mucosa. Outside the submucosa is the muscularis externa (propria), which is organized as two distinct layers of smooth muscle, an inner layer oriented circularly and an outer layer oriented longitudinally with respect to the long axis of the gut. Both of these layers are substantially thicker than the muscularis mucosa. External to this is the connective tissue serosa. At the boundary between the submucosa andmuscularis externa, and between the two layers of smooth muscle, small collections of neurons of the entericnervous system are found. These are the submucosal plexus and the myenteric plexus respectively.

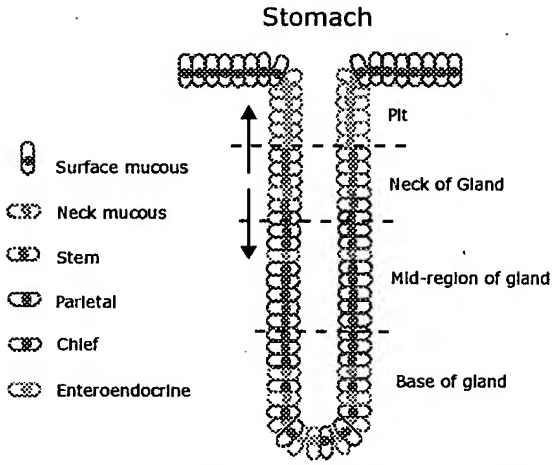
This general structure varies somewhat from region to region of the gut. Consult the lecture notes for more details.

GIT - Some regional variations

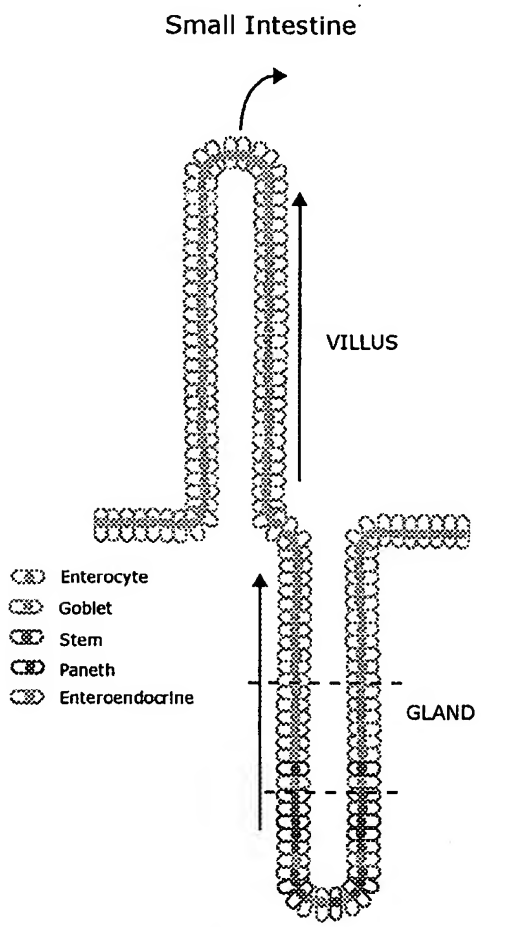




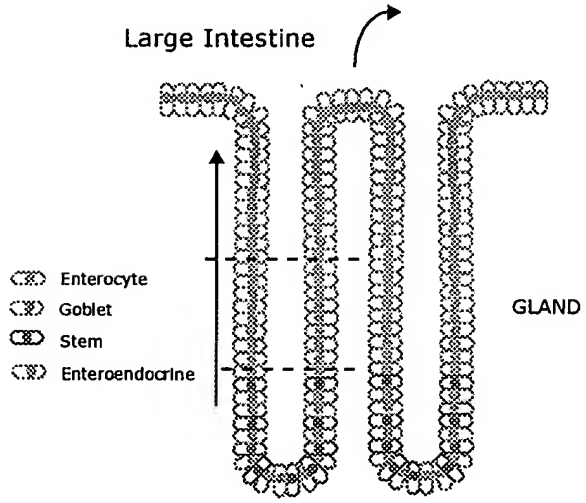
In the large intestine, the continuous outer longitudinal layer of smooth muscle of the muscularis externa is replaced by three thickened strips of longitudinally oriented smooth muscle, the taenia coli.



Schematic showing the distribution of cells in gastric glands of the fundus and body. The cells are not all the same shape as shown here. Consult lecture notes for more details.

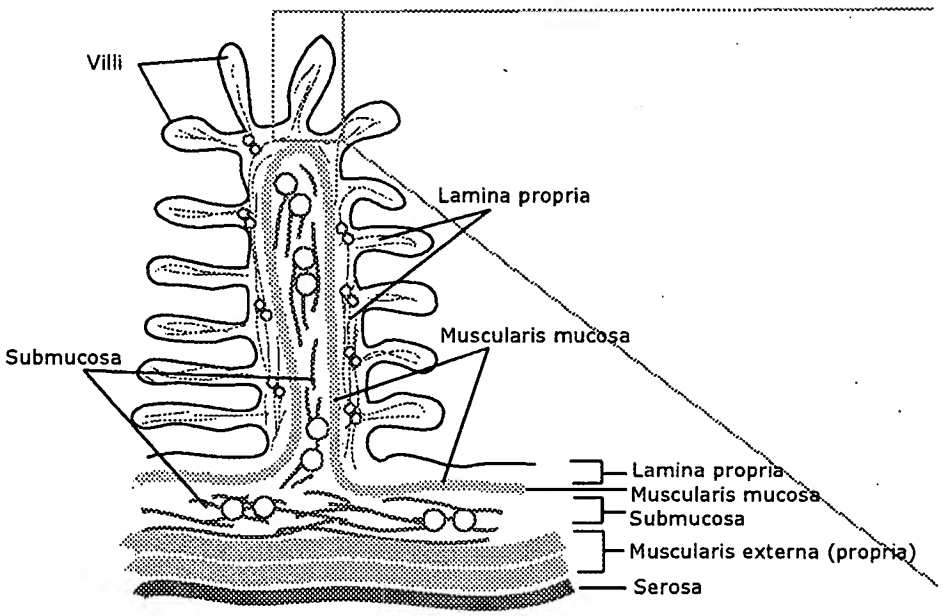


Schematic diagram of the distribution of cells in villi and glands of the small intestine. Not all of cells are the same shape as shown here. Consult lecture notes for more details.

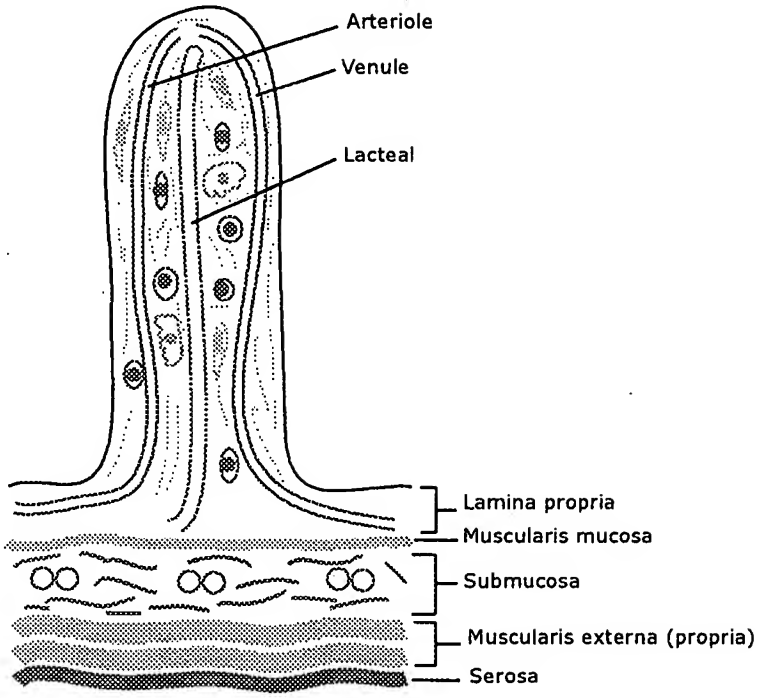


Schematic diagram of the distribution of cells in the glands of the small intestine. Not all of cells are the same shape as shown here. Consult lecture notes for more details.

Mucosal folds in the small intestine



Plica circularis, a permanent fold in the wall of the small intestine. The core of the plica is submucosa. Note the muscularis mucosa follows the fold. Villi project from the plica. Epithelium not shown.



A villus, a mucosal fold of the small intestine. The core of the villus is lamina propria; the muscularis mucosa does not penetrate the fold. Each villus has an extensive capillary bed (not shown), supplied by an arteriole and drained by a venule. A single blind-ended lymphatic vessel, the lacteal, is also found in the core of each villus. Immune cells and connective tissue cells are numerous in the lamina propria core. Epithelium not shown.

GASTROINTESTINAL TRACT

GENERAL STRUCTURE

* Composed of four layers
  - Inner epithelial *mucosal* layer
  - Middle connective tissue *submucosal* layer
  - Smooth muscle *muscularis* layer
    - Inner circular
    - Outer longitudinal
  - Outer *adventitial* connective tissue layer
    - Blends with CT of adjacent structures
  - Where the gut is *peritonealized* the adventitia is covered with *mesentery*
  - *Mesentery is a layer of simple squamous mesothelial* cells
* Variations in thickness and exact structure between parts of the gut

OESOPHAGUS

* Epithelium is stratified squamous non-keratinized
* Muscle type varies according to position
  - upper 1/3 is *skeletal*
  - lower 1/3 is *smooth*
  - middle 1/3 is *mixed*
* Oesophageal *mucous glands* in submucosa
* At junction with stomach, *cardiac glands* in lamina propria
  - identical to cardiac glands of the stomach
  - secrete mucous and lysozyme, occasional acid secreting cells
* Epithelium in distal portion may undergo *metaplasia* in response to acid damage

SEARCH NOTES

The Small Intestine

The small intestine is the largest component of the digestive tract and the major site of digestion and absorption. In addition to receiving chyme from the stomach, the initial segment of the small intestine, the duodenum, receives bile from the gall bladder and digestive enzymes from the pancreas. The pancreatic enzymes are produced in an inactive form and only become active in the lumen of the duodenum.

The small intestine is divided into three parts, the **duodenum** (25 cm), the **jejunum** (2.5 m) and the **ileum** (3.5 m).

Mucosa:

The mucosa of the small intestine is highly modified. The luminal surface is completely covered by a number of finger- or leaf-like projections called **villi**, 0.5-1.5 mm in length. The core of a villus is an extension of the lamina propria, and its surface is covered by a simple columnar epithelium. Opening onto the luminal surface at the bases of the villi are simple tubular structures called **intestinal glands** or **crypts of Lieberkuhn**. The crypts extend downward toward the muscularis mucosae. The simple columnar epithelium lining them is continuous with that covering the villi.

The predominant cell type of the epithelium is the **enterocyte** or **absorptive cell**. Each enterocyte has about 3000 **microvilli** at its luminal surface, which appear in the light microscope as the fuzzy striated border on the surface of the villi. [Electron microscopy: Microvilli are cylindrical protrusions, about 1 micrometer tall, of the cell membrane enclosing a core of filaments, mostly actin filaments. The actin filaments attach to the plasma membrane at the tip of the microvillus and end in the terminal web near the base of the microvillus. The terminal web consists of actin microfilaments and myosin, and is attached to the zonula adherens of the junctional complex binding epithelial cells to one another near their apical ends.]

The villi and microvilli, together with folds in the submucosa called plicae circulares (below), increase the absorptive surface of the small intestine about 600 times.

The epithelium of the small intestine consists of the following cell types:

- **Enterocytes** or **absorptive cells**. These are tall columnar cells with microvilli and a basal nucleus, specialized for the transport of substances. They are bound to one another and other cell types by junctional complexes (zonula occludens or tight junction, zonula adherens, and macula adherens). Amino acids and monosaccharides are absorbed by active transport, monoglycerides and fatty acids cross the microvilli membranes passively. Absorbed substances enter either the fenestrated capillaries in the lamina propria just below the epithelium, or the lymphatic lacteal (most lipids and lipoprotein particles). Enterocytes have a lifespan of about 5-6 days.

- **Goblet cells**. These mucus-secreting cells are the second most abundant epithelial cell. They are found interspersed among the other cell types. Their mucous is a very large glycoprotein that accumulates at the apical end of the cell, rendering it wide. The slender base of the cell hold the nucleus and organelles. Goblet cells usually appear pale or empty due to the loss of their contents upon preparation. However their glycoprotein content can be revealed with special stains (such as the PAS stain in slide #9). The abundance of goblet cells increases from the duodenum to the terminal ileum. Their lifespan is also 5-6 days.

- **Paneth cells**. Paneth cells are found only in the bases of the crypts of Lieberkuhn. These cells have an oval basal nucleus and large, refractile acidophilic granules at their apical end. The granules contain the antibacterial enzyme lysozyme, other glycoproteins, an arginine-rich protein and zinc, an essential trace metal for a number of enzymes. Paneth cells also phagocytize some bacteria and protozoa. They may have a role in regulating intestinal flora. They have a lifespan of about four weeks. Paneth cells are easy to identify with the light microscope.

- **Enteroendocrine cells**. These cells were described in the section on the stomach. In the intestine, they are most often found in the lower part of the crypts but can occur at all levels of the epithelium. Their most abundant products here are **cholecystokinin** or **CCK**, which stimulates pancreatic enzyme secretion and gall bladder contraction, **secretin**, which stimulates pancreatic and biliary bicarbonate secretion, and **gastric inhibitory peptide** or **GIP**, which inhibits gastric acid secretion. As in the stomach, these cells are not easily seen without special preparations.

- **M** or **microfold cells**. These cells are epithelial cells that overlie Peyer's patches and other large lymphatic aggregations. They are relatively flat and their surface is thrown into folds, rather than microvilli. They endocytose antigens and transport them to the underlying lymphoid cells where immune responses to foreign antigens can be initiated. We do not identify M cells in the lab.

- **Undifferentiated cells**. These stem cells are found only at the base of the crypts and give rise to all the other cell types. A cell destined to be a goblet cell or enterocyte undergoes about 2 additional divisions after leaving the pool of stem cells, and migrates from the crypt to the villus. It will be shed at the tip of the villus.

Special stains for glycoproteins reveal the **glycocalyx** at the surface of the intestinal epithelium. The glycocalyx consists of glycoprotein enzymes inserted into the plasma membrane of enterocytes, with their functional groups extending outward. These enzymes are secreted by the enterocytes themselves. They include **peptidases** and **disaccharidases**, as well as **enterokinase** (or **enteropeptidase**), which converts (inactive) trypsinogen to (active) trypsin. Trypsin, in turn, activates trypsinogen itself as well as other pancratic zymogens.

Lymphocytes are sometimes seen in the intestinal epithelium. They are thought to be sampling antigens in the epithelial intercellular spaces. It is believed that they process the antigens before returning to lymphatic nodules in the lamina propria and undergoing blastic

transformation, leading to antibody secretion by the newly differentiated plasma cells.

Within the lamina propria core of each villus is a lymphatic capillary called a lacteal, as well as numerous capillaries. The lacteal is accompanied by smooth muscle fibres arising from the muscularis mucosae. The smooth muscle in the villus allows it to contract intermittantly, expelling the contents of the lacteal into the lymphatic network surrounding the muscularis mucosae. The lamina propria is very cellular, with numerous lymphocytes, plasma cells, macrophages and eosinophils. Lymphatic nodules are quite common and are an important component of GALT. Lymphatic nodules arising in the lamina propria may extend into the submucosa. The muscularis mucosae may be partially or totally disrupted by the nodules. ***The ileum is characterized by having large aggregates of lymph nodules, called Peyer's patches, in the submucosa.*** (Unfortunately we have no slides of the ileum, but you should know the term Peyer's patches. Look at pictures in an atlas.)

The muscularis mucosae of the small intestine consists of an inner circular and outer longitudinal layer of smooth muscle.

Submucosa:

The submucosa consists of dense connective tissue. Adipose cells may be present. Both the duodenum and the jejunum are characterized by modifications of the submucosa. (So is the ileum, although its modification, Peyer's patches, arises from the lamina propria.)

The duodenum is distinguished by the presence of Brunner's glands, which occupy most of the submucosa. In some areas these glands may penetrate the muscularis mucosae to enter the lamina propria. Brunner's glands are branched tubuloalveolar glands that produce a clear, viscous, alkaline (pH 8.1-9.3) fluid, containing neutral and alkaline glycoproteins and bicarbonate ions. (Because of the glycoproteins, Brunner's glands also react with the PAS that stains the goblet cells and glycocalyx in slide 9). The secretion of Brunner's glands protects the proximal small intestine by neutralizing the acidic chyme from the stomach. It brings the pH of the intestinal contents close to the optimum for the pancreatic digestive enzymes delivered to the stomach.

The jejunum is characterized by the presence of numerous, large folds in the submucosa, called plicae circulares (aka valves of Kerckring). The plicae consist of a core of submucosa and the overlying mucosa. They have a semilunar, circular or spiral form and extend about one-half to two-thirds around the circumference of the lumen. Although they may be present in the duodenum and ileum, they are not as large and are not a significant feature in those regions.

Muscularis Externa:

The muscularis externa is as described under General Structure. The two layers (inner circular for mixing and outer longitudinal for peristalsis) are well organized. Features such as Auerbach's plexus tend to be easy to find.

Adventitia or Serosa:

Either a serosa or an adventitia may be present.

Fig. 21 Low power view of the duodenum

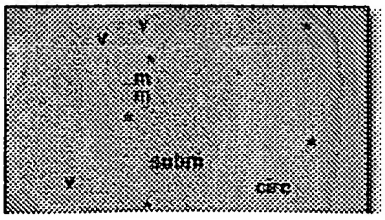


Figure 21 shows a low power view of the complete wall of the duodenum. The villi appear packed together and only a few (labelled) can be seen distinctly. The crypts at their bases are not identifiable. The mucosa can be distinguished from the submucosa because of the abundance of Brunner's

glands in the latter; they have picked up the PAS stain and appear as red circles. The muscularis mucosae is not readily seen at this magnification (and is frequently disrupted by Brunner's glands); its approximate course is shown by asterisks. There is a tear at the top of the figure where much of the submucosa has torn away from the muscularis externa, whose circular and longitudinal layers can be distinguished. The boundary is indicated by asterisks. The serosa or adventitia is not identifiable. All pictures of the duodenum shown here are taken from slide 9.

Fig. 22 Duodenal mucosa and submucosa

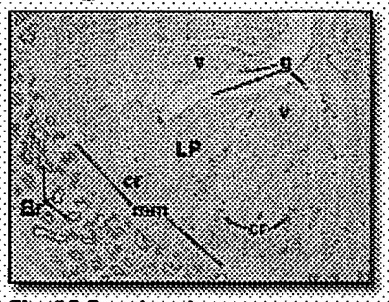


Fig. 22 Duodenal mucosa and submucosa

Figure 22 shows a slightly higher power view of the duodenal mucosa and submucosa. The individual villi can be distinguished, and some crypts can be seen at their bases. Goblet cells, staining red, can be seen in the epithelium of both the villi and the crypts. The glycocalyx can be faintly seen as a pink line running along the surface of the epithelium. The lamina propria forming the core of the villi and lying between the crypts contains numerous lymphocytes and other cells. The muscularis mucosae can be distinguished as a pink band.

An abundance of Brunner's glands can be seen in the submucosa. They have not broken through to the mucosa in the section shown, and the muscularis mucosae remains undisrupted. Brunner's glands open into the intestinal lumen through ducts (not seen here).

Fig 23 Close-up of duodenal villus

Figure 23 shows a high power view of the top part of one villus and part of an adjacent villus. The nuclei of the simple columnar epithelium are lined up in a row at the base of the cells. Goblet cells are interspersed among the enterocytes. At this magnification, the glycocalyx can be readily identified.

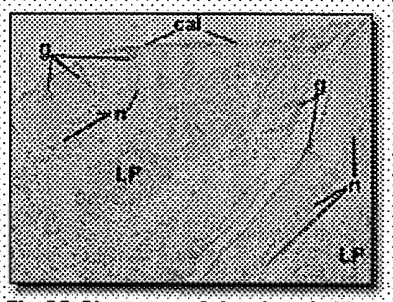


Fig 23 Close-up of duodenal villus

Fig. 24 Close-up of duodenal crypt

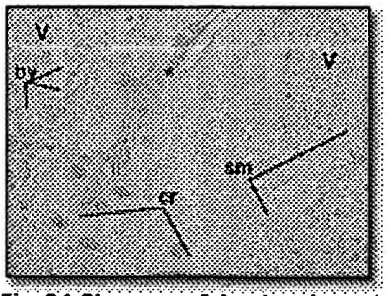


Fig. 24 Close-up of duodenal crypt

Figure 24 shows a crypt opening into the lumen between the bases of two villi. The epithelium lining the inside of the crypt can be seen to be continuous with that lining the outside of the villi. Enterocytes and goblet cells are present in crypts and villi. The lumen can be seen at the top of the crypt, but is obscured at its base. The base of the crypt ends just beyond the field of view at the bottom left. To the right of the crypt, part of another crypt, sectioned obliquely, is seen as the top half of a circular profile.

Many lymphoid cells are seen in the lamina propria. Some blood vessels can also be seen, as can strands of smooth muscle, which arise from the muscularis mucosae and are principally associated with the lacteal (not seen here).

Fig. 25 Muscularis externa of the duodenum

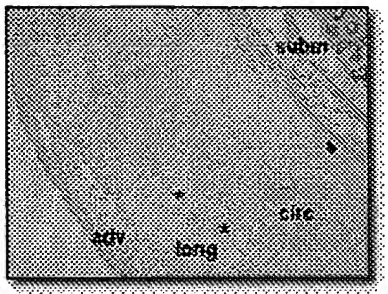


Fig. 25 Muscularis externa of the duodenum

Figure 25 shows the regularly-arranged muscularis externa of the duodenum. The inner circular layer is larger than the outer longitudinal layer. An Auerbach's plexus lies between the two layers (barely identifiable at this magnification). The connective tissue of the adventitia (or serosa) lines the outer surface, and a bit of the submucosa (with Brunner's glands) is seen beyond the inner circular layer. The big gap between submucosa and muscularis externa is an artifact (tear).

Fig. 26 Small Auerbach's plexus in the duodenum

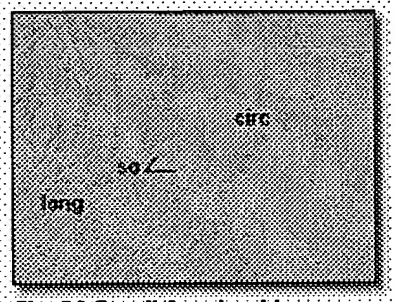


Fig. 26 Small Auerbach's plexus in the duodenum

Figure 26 shows a high power view of an Auerbach's plexus in the duodenum. Two nerve cells bodies can be seen.

Fig. 27 Plica circularis in duodenum

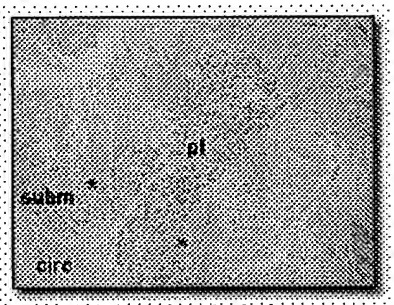


Fig. 27 Plica circularis in duodenum

Figure 27 is a low power view of a plica circulares in the duodenum. This large fold in the submucosa raises the overlying mucosa with its villi and crypts.

Fig. 28 Low power view of the jejunum

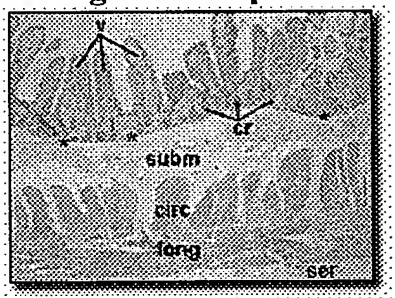


Fig. 28 Low power view of the jejunum

Figure 28 shows a low power view of the jejunum (from slide 39). The mucosa, submucosa and muscularis externa are shown completely, a bit of the serosa or adventitia is shown at the lower right. One of the villi (to the right of the labelled ones) is folded over on itself. Note the absence of Brunner's glands in the submucosa. A few blood vessels can be seen at this magnification. No plicae circulares are included in the field of view. In the muscularis mucosae, the circular and longitudinal layers seem reversed; this is a phenomenon of sectioning.

Fig. 29 Plica circularis in jejunum

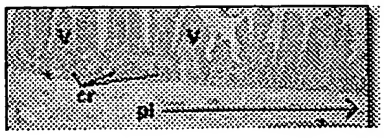


Figure 29 is at the same magnification as Figure 28, but shows an area of the jejunum in which a plica is present.

Only the mucosa, submucosa and a very small part of the inner layer of the muscularis externa are seen. The plica continues to the right beyond the field of view. Compare this plica to the one shown in the duodenum in Figure 27. The plicae in the jejunum tend to be taller and thinner. They are also more frequent. If you scan your own slide 39 you might find branching plicae or plicae arising from other plicae.

Fig. 30 Villi and crypts in the jejunum

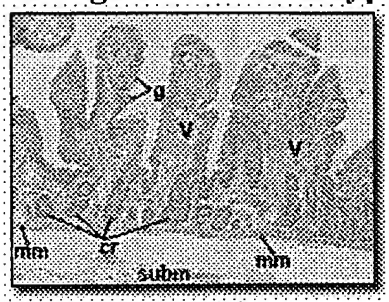


Fig. 30 Villi and crypts in the jejunum

Figure 30 shows a medium power view of the mucosa (and a bit of the submucosa) of the jejunum. The muscularis mucosae can be seen as a continuous band. Some of the crypts can be seen to be emptying into the bases of the villi, others, sectioned obliquely, appear as circular profiles. The epithelium appears as a darker red line outlining the villi and continuing into the crypts. The little pale "holes" in the epithelium are goblet cells.

Fig. 31 Lacteal and smooth muscle strand in a villus in jejunum

Figure 31 shows a high power view of part of a villus. The epithelium is not very edifying as it is sectioned obliquely and is several layers thick. A few goblet cells can nevertheless be distinguished. However, both the central lacteal (as a cross section) and the smooth muscle strand accompanying it can be seen clearly among the lymphocytes in the lamina propria.

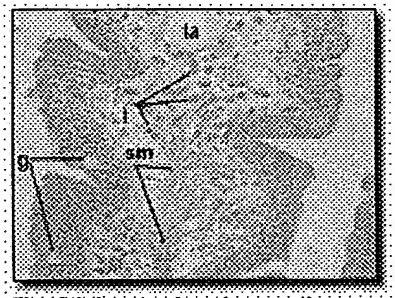


Fig. 31 Lacteal and smooth muscle strand in a villus in jejunum

Fig. 32 Paneth cells at base of crypts

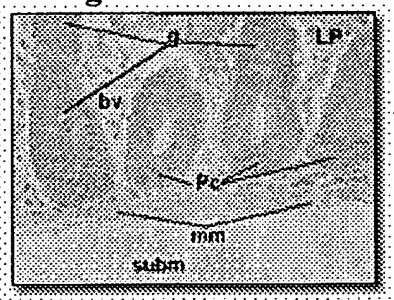


Fig. 32 Paneth cells at base of crypts

Figure 32 shows a high power view of some crypts in the jejunum. Paneth cells, with refractile granules, are seen at the bases of the crypts (the only place they're found). The Paneth cells on your slides show up much more clearly than on this computer image. Some goblet cells are also seen in the epithelium. The other cells are enterocytes (absorptive cells). The muscularis mucosae can be readily seen. A bit of the submucosa is present but is bleached out (as a result of trying to get Paneth cells to show up on computer image).

Fig. 33 Auerbach's plexus in the jejunum

Figure 33 shows an Auerbach's plexus between the two layers of the muscularis externa in the jejunum. This sections happens to have gone through the nucleus and nucleolus of several nerve cell bodies (somata). The nucleus is a paler structure lying in the nerve cell body, the nucleolus appears as a brighter dot. The borders of the nerve cell bodies themselves are a bit hard to see; two of them are

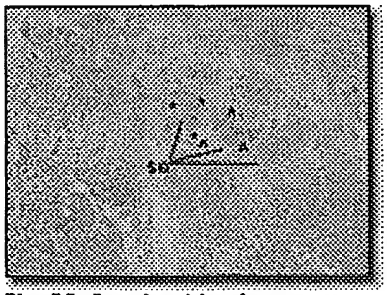


Fig. 33 Auerbach's plexus in the jejunum

outlined with different symbols.

Gastrointestinal

Alimentary Canal

- Discussion of General Structure
- Esophagus
- Stomach
- Small Intestine
- Large Intestine

Organs of Digestion

- Salivary Glands
- Pancreas
- Liver
